

17



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,253	12/10/2001	Luca Rastelli	21402-042 (CURA-342)	4494

7590 05/17/2004

Ivor R. Elrifi
MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY AND POPEO, P.C.
One Financial Center
Boston, MA 02111

EXAMINER

RAWLINGS, STEPHEN L

ART UNIT	PAPER NUMBER
----------	--------------

1642

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/016,253

Applicant(s)

RASTELLI ET AL.

Examiner

Stephen L. Rawlings, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9 and 20-23 is/are pending in the application.
- 4a) Of the above claim(s) 20-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 8,9 and 20-23 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>20030807</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The election filed February 23, 2004 is acknowledged and has been entered. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant has elected the invention of claims 8 and 9, insofar as the claims are drawn to a method for identifying a therapeutic agent, or a candidate therapeutic agent for treating a tuberous sclerosis complex associated disorder in a subject, wherein said method comprises measuring the expression of the nucleic acid molecule, TSC 122.

2. Claims 8, 9, and 20-23 are pending in the application. Claims 20-23 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 8 and 9 are currently under prosecution.

Election/Restrictions

4. Newly submitted claims 20-23 are directed to an invention that is independent or distinct from the elected invention for the following reasons:

Claims 8 and 9 are drawn to a method for identifying a candidate therapeutic agent or an individualized therapeutic agent comprising measuring the expression the nucleic acid molecule, TSC 122; whereas claims 20-23 are drawn to a method for identifying a candidate therapeutic agent comprising screening agents to determine if the agent binds the polypeptide encoded by the nucleic acid molecule, TSC 122. Thus, the invention of claims 8 and 9 and the invention of claims 20-23 are distinct from one another, because the inventions are materially different and comprise different steps. In addition, the search required to examine the invention of claims 8 and 9 is not co-extensive with the search required to examine the invention of claims 20-23, such that having to search both inventions would constitute a serious burden. Because

Art Unit: 1642

inventions are distinct and the search required to examine the invention of claims 8 and 9 is a different from the search required to examine the invention of claims 20-23, restriction is proper.

Since Applicant has received an action setting forth a restriction of the originally presented claims and elected claims directed to one of the restricted inventions, the merit of the claims directed to the elected invention have been considered herein. Accordingly, claims 20-23 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Information Disclosure Statement

5. The information disclosure filed August 7, 2003 has been considered. An initialed copy is enclosed.

Receipt of the information disclosure filed March 16, 2004 is acknowledged; however, because the electronic images of the disclosure and the attached references have not yet been made, the information cannot be presently considered. Accordingly, the information disclosed will be considered after Applicant has responded to this Office action.

Oath/Declaration

6. The declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because non-initialed and non-dated alterations have been made to the declaration at page 3. See 37 CFR § 1.52(c).

Specification

7. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks

should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include: GenBank™ (page 57, line 26); Perkin Elmer™ (page 57, line 29; page 58, line 26); Apple™ (page 58, line 27); Macintosh™ (page 58, line 27); TaqMan™ (page 60, line 31; page 63, Table 2; page 64, Table 3); and Clontech™ (pages 64-65, Table 3).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

8. The specification is objected to because of the following informalities:
- (a) At page 3, line 17, the Shimkets et al. reference should read, "798-803". Appropriate correction is required.
 - (b) At page 3, line 18, "embryonic" is misspelled. Appropriate correction is required.
 - (c) At page 3, line 22, "polypeptides" is misspelled. Appropriate correction is required.
 - (d) At page 3, line 26, the disclosure reads, "identify understand". Appropriate correction is required.
 - (e) At page 3, line 27, the disclosure reads, "it was identify". Appropriate correction is required.
 - (f) Throughout the specification, e.g., page 61, line 7, sentences are not properly punctuated with periods. Appropriate correction is required.
 - (g) The upper margin at page 63 is not of the correct size. As a result of punching holes in the sheet so as to attach it to the file, information contained thereon has been lost; therefore, a replacement sheet is required.

9. The specification is objected to because of the following matter:

Beginning at page 57, line 25, the specification discloses an example in which the expression of antileukoprotease (ALP) is compared in various tissues; however, at page 57, line 26, the disclosure reads, "quantitative expression of NMB (GenBank Accession No: X04470; Table 1; TSC)". GenBank™ Accession No. X04470 is the polynucleotide sequence of a human messenger RNA (mRNA) molecule encoding antileukoprotease (ALP), which was isolated from cervix uterus; see the attached printout of Database NCBI (GENBANK), Accession No. X04470, Version X04470.1 GI:28638, 21 March 1995. Contrary to the disclosure at page 57, line 25, ALP is not alternatively designated "NMB". Accordingly, it is objectionable that the disclosure uses "NMB", rather than antileukoprotease, when referring to the results of the analysis at, e.g., page 60, line 21. Moreover, it is objectionable that the disclosure uses "NMB" to designate more than one nucleic acid molecule, since "NMB" is used at page 57 to designate ALP and at page 9, Table 1, also used to designate TSC 122, or GenBank™ Accession No. AJ251685. Furthermore, although the disclosure at page 57, line 26, reading, "quantitative expression of NMB (GenBank Accession No: X04470; Table 1; TSC)", suggests antileukoprotease (ALP), or GenBank™ Accession No: X04470 should be listed in Table 1, the table does not appear to disclose any information regarding the nucleic acid molecule.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 8 and 9 are drawn to a method for identifying a therapeutic agent, which can be used to treat a tuberous sclerosis complex associated disorder.

The amount of guidance, direction, and exemplification set forth in the specification would not be sufficient to enable the skilled artisan to practice the claimed invention with a reasonable expectation of success without having to first perform an undue amount of additional experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to a method comprising determining if a test agent affects the level of expression of the nucleic acid molecule of "TSC 122". However, the specification fails to teach how the practitioner should select a therapeutic agent after determining the difference in the level of expression of TSC 122 in the test cell population and the reference cell population. Moreover, the skilled artisan could not reasonably expect to successfully identify a therapeutic agent for treating a tuberous sclerosis complex associated disorder without first performing an undue amount of experimentation to determine how the expression of TSC 122 correlates with the onset and/or progression of each of the disorders encompassed by the claims. In addition, the skilled artisan could not reasonably expect to successfully practice the claimed invention without first determining how a therapeutic agent for treatment of each disorder should alter the expression of TSC 122, i.e., without determining whether a given agent should promote or inhibit expression of TSC 122, and then whether promoting or inhibiting the expression of TSC 122 actually provides therapeutic benefit to a patient having any one of the disorders encompassed by the claims. Thus, the

amount of experimentation that would have to be performed before the claimed invention could be practiced with a reasonable expectation of success would not be merely routine or conventional.

The specification teaches at page 9, "TSC 122" or "NMB" is the nucleic acid molecule of GenBank™ Accession No. AJ251685. However, the specification does not appear to teach if TSC 122 is differentially expressed in Tsc2-/+ or Tsc2-/- mice, as compared to Tsc2+/+ mice, or how it is differentially expressed. While the 5th column of Table 1 (page 9) indicates the ratio of the level of TSC 122 expression in embryonic fibroblasts of Tsc2-/+ mice to the level in Tsc2+/+ mice, the table lists the value, "-4". It cannot be determined how the ratio can be a negative number. If the nucleic acid molecule is overexpressed in Tsc2-/+ mice relative to Tsc2+/+ mice, the value of the ratio should be greater than one, but the value should be a positive number. If the nucleic acid molecule is underexpressed in Tsc2-/+ mice relative to Tsc2+/+ mice, the value of the ratio should be smaller than one, but still the value should be a positive number. Because the tabulated value is a negative number it cannot be determined if TSC 122 is differentially expressed in Tsc2-/+ embryonic fibroblasts, as compared to the embryonic fibroblasts of Tsc2+/+ mice, or how it is differentially expressed. The 6th column of Table 1 supposedly indicates the ratio of the level of TSC 122 expression in embryonic fibroblasts of Tsc2-/- mice to the level in Tsc2+/+ mice, but lists "X" in the row corresponding to TSC 122. The key at page 10 indicates "X" means "no poison"; it cannot be determined "no poison" is relevant to the data that is supposedly tabulated in Table 1, but "X" is clearly not representative of the value of the ratio of the level of TSC 122 expression in Tsc2-/- mice to the level in Tsc2+/+ mice. Therefore, it cannot be determined if TSC 122 is differentially expressed in the embryonic fibroblasts of Tsc2-/- mice, as compared to the embryonic fibroblasts of Tsc2+/+ mice. The 8th column of Table 1, which supposedly indicates the ratio of the level of TSC 122 expression in neuronal stem cells of Tsc2-/- mice to the level in Tsc2+/+ mice, lists "NEW" in the row corresponding to TSC 122. The key at page 10 indicates "NEW" means "de novo expression". The term "*de novo*" is often applied to particular biochemical pathways in which metabolites are newly biosynthesized (e.g., *de novo* purine biosynthesis), so

while the table appears to indicate TSC 122 is newly synthesized, it cannot be determined whether TSC 122 is differentially expressed, or to what extent, in the neuronal stem cells of Tsc2^{-/-} mice, relative to those of Tsc2^{+/+} mice. As noted above, the skilled artisan could not reasonably expect to successfully identify a therapeutic agent for treating a tuberous sclerosis complex associated disorder without first determining how the expression of TSC 122 correlates with the onset and/or progression of each of the disorders encompassed by the claims and then determining how, and to what extent, a therapeutic agent for treatment of each disorder should alter the expression of TSC 122, because otherwise the skilled artisan could not know how to identify a test agent that has a desirable effect upon the expression of TSC 122. The 7th column of Table 1 indicates expression of TSC 122 in the neuronal stem cells of Tsc2^{-/-} mice and Tsc2^{+/+} mice does not differ, since the ratio of the levels of expression is 1.0, so the skilled artisan would not expect the expression of TSC 122 to correlate with the onset or progression of a tuberous sclerosis associated disorder affecting neuronal cells; nevertheless, the claimed invention cannot be used with a reasonable expectation of success without knowing how a test agent should affect the expression of TSC 122 without knowledge of whether it is therapeutically effective to increase or decreases its expression.

Additionally, drug discovery is a highly unpredictable art. Gura (*Science* **278**: 1041-1042, 1997) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile (abstract). Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs). Gura discloses that often researchers merely succeed in developing a therapeutic agent that is useful for treating the animal or cell that has been used as a model, but which is ineffective in humans, indicating that the results acquired during pre-clinical studies are often non-correlative with the results acquired during clinical trials (page 1041, column 2). For example, Gura very succinctly teaches, "xenograft tumors don't behave like naturally occurring tumors in humans" (page 1041, column 2).

Although researchers had hoped that xenografts would prove to be better models for studying cancer in humans and screening candidate therapeutic agents for use in treating patients diagnosed with cancer, Gura discloses, "the results of xenograft screening turned out to be not much better than those obtained with the original models". Gura states that as a result of their efforts, " '[w]e had basically discovered compounds that were good mouse drugs rather than good human drugs' ".

Although the teachings of Bergers et al. (*Current Opinion in Genetics and Development* 10: 120-127, 2000) are drawn to specific antitumor agents, namely matrix metalloproteinase inhibitors, the great extent of unpredictability in the art of drug discovery is further underscored by the disclosures of Berger et al. Bergers et al. teaches, "a body of data over the past few years indicate [...] that proteinases and proteinase inhibitors may, under special circumstance, either favor or block tumor progression. For example, ectopic expression of TIMP-1 [a natural inhibitor of metalloproteinases] allows for some tumors to grow, while inhibiting others" (page 125, column 2). In fact, Bergers et al. discloses the Bayer Corporation recently halted a clinical trial of a metalloproteinase inhibitor because patients given the drug experienced greater progression of cancer than did patients given a placebo (page 125, column 1). Bergers et al. comments, "these results are somewhat surprising and contrary to Bayer's preclinical data, which confirmed that the drug inhibited tumor activity in rodents" (page 124, columns 1-2). Bergers et al. also teaches that the absence of a metalloproteinase activity in mice actually predisposes the mice to *de novo* squamous carcinomas. Thus, one skilled in the art cannot often reliably and accurately predict the effect of administering a pharmaceutical composition purported to have a desired pharmacological effect to a subject. Generally the efficacy of any unproven drug must be determined empirically.

The disclosed invention was conceived in view of Applicant's finding that certain genes, including presumably TSC 122, are differentially expressed in the cells of mice lacking one or both alleles of the tuberlin-encoding gene, *TSC2*, which has been associated with tuberous sclerosis complex, an autosomal dominant genetic disease. Because the *TSC2* gene is associated with tuberous sclerosis complex, Applicant has

speculated an agent that affects the expression of another gene affected by the loss of expression of TSC2 might have therapeutic value. However, in view of the teachings of Gura and Bergers et al., it is submitted, absent a showing otherwise, that one cannot reasonably extrapolate the teachings of the specification to successfully use the claimed invention to identify a therapeutic agent without having to first perform an undue amount of experimentation to determine if the model used by Applicant reliably predicts the effectiveness of an agent in treating any of the tuberous sclerosis associated disorders to which the claims refer. An undue amount of additional experimentation would have to be performed before the skilled artisan could have a reasonable expectation of success in practicing the claimed invention to identify a therapeutic agent for treatment of a tuberous sclerosis complex associated disorder.

Furthermore, because the manifestations of tuberous sclerosis complex are highly variable, it cannot be predicted whether an agent that affects the expression of TSC 122 in a given cell population can be used to treat each and every manifestation of the disease. Lendvay et al. (*Journal of Urology* 169: 1635-1642, 2003) reviews the pathology of tuberous sclerosis complex and teaches there are neurological, dermatological, renal, cardiovascular, pulmonary, ocular, and other manifestations of the disease; see, e.g., page 1640, Appendix 1. As each manifestation of the disease affecting different organ or tissue sites is likely associated with the altered expression of a different gene or a different set of genes, without knowing which manifestations of the disease are associated with the abnormal expression of TSC2 in humans, leading to altered expression of TSC 122, the skilled artisan cannot predict whether an agent that affects the expression of TSC 122 might have therapeutic value in treating different manifestations of the disease, or the different disorders associated with the disease. Moreover, while the specification shows differential expression of genes in embryonic fibroblasts and neuronal stem cells of TSC2-/+ , TSC-/- , and TSC+/+ mice, there is no showing that the expression of TSC 122 is abnormally expressed in other types of cells in TSC2-deficient mice, such as retinal and renal cells. Accordingly, the expression of TSC 122 cannot be correlated with the incidence of non-neurological, non-dermatological manifestations of the disease; and there is no factual evidence to

support the assertion that an agent that affects the expression of TSC 122 in any and all test cells can be used as a therapeutic agent to treat the disease or its associated disorders.

For all of the above reasons, Applicant's disclosure of the claimed invention is too inadequate to enable the skilled artisan to use the claimed invention as required under the provisions of 35 USC § 112, first paragraph.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite because the preamble recites: "A method for identifying a candidate therapeutic agent", whereas the body of the claim recites, "thereby identifying a therapeutic agent". As a candidate therapeutic agent is not necessarily therapeutic agent, the metes and bounds of the subject matter that Applicant regards as the invention cannot be ascertained. If Applicant regards the invention as a method for identifying a candidate therapeutic agent, this ground of rejection can be obviated by amending claim 8 by insertion of "candidate" before "therapeutic agent" in line 14. If Applicant regards the invention as a method for identifying a therapeutic agent, amending claim 8 to delete "candidate" from line 1 can obviate this ground of rejection.

Claims 8 and 9 are indefinite because the claims use of the designations "TSC 122" as the sole means of identifying the nucleic acid molecule to which the claims refer. The use of laboratory designations only to identify a particular nucleic acid molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct nucleic acid molecules. It is noted the specification discloses at page 9 in Table 1 that "TSC 122" is otherwise designated "NMB", which is the nucleic acid molecule identified by GenBank™ Accession No. AJ251685; however, the polynucleotide sequence identified by any accession number is

Art Unit: 1642

subject to revision and change. Therefore, the reference to an accession number does not resolve the present issue. Because the polynucleotide sequence of a nucleic acid molecule is a unique identifier that unambiguously defines a given nucleic acid molecule, amending claims 8 and 9 to include the polynucleotide sequence of the nucleic acid molecule by recitation of a specific sequence identification number corresponding to the same polynucleotide sequence set forth in the Sequence Listing can obviate this rejection.

Conclusion

14. No claims are allowed.

15. The art made of record and not relied upon is considered pertinent to Applicant's disclosure. Kalow et al. reviews pharmacogenetics and personalized medicine. Rininger et al. reviews differential gene expression technologies for identifying surrogate markers of drug efficacy and toxicity. Mancinelli et al. reviews pharmacogenomics and the promise of personalized medicine.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

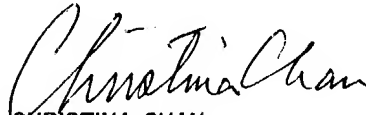
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, Ph.D. can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1642

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
May 12, 2004


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600